UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,153	10/09/2006	Suzana Rosic-Kablar	14096.0056USWO	3182

23552 7590 10/14/2008

MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
HILL, KEVIN KAI	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
10/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,153	ROSIC-KABLAR ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *7-27,29-35,37 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,28 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *December 23, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant's response to the Requirement for Restriction, filed on August 11, 2008 is acknowledged. Applicant has elected the invention of Group I, claim(s) 1-6, 28 and 36, drawn to undifferentiated canine embryonic stem cells.

Election of Applicant's invention(s) was made with traverse, arguing that it would not be unduly burdensome to search and examine all pending claims.

Applicants' arguments have been fully considered but are not found persuasive. MPEP §803 states that "If the search and examination of all the claims in an application can be made without serious burden, the Examiner must examine them on the merits, even though they include claims to independent or distinct inventions."

In the instant case a serious burden exists since each limitation, directed to business methods, primer sequences, and differentiated canine cells, requires a separate, divergent, and non co-extensive search and examination of the patent and non-patent literature. Further, a search and examination of all the claims directed to both embodiments involves different considerations of novelty, obviousness, written description, and enablement for each claim. In view of these requirements, it is the Examiner's position that searching and examining all of the claims in the same application presents a serious burden on the Examiner for the reasons given above and in the previous Restriction Requirement.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-27, 29-35 and 37-38 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1-6, 28 and 36 are under consideration.

Priority

This application is a 371 of PCT/CA04/00456 filed on March 26, 2004. Applicant's claim for the benefit of a prior-filed application parent provisional application 60/458863 filed on March 28, 2003 and 60/526385 filed on December 1, 2003 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Accordingly, the effective priority date of the instant application is granted as March 28, 2003.

Information Disclosure Statement

Applicant has filed Information Disclosure Statements on December 23, 2005 that has been considered. The signed and initialed PTO Form 1449 is mailed with this action.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the Examiner on form PTO-892, they have not been considered.

Specification

1. **The disclosure is objected to because of the following informalities:** Figure 5 comprises panels A-C. However, the Brief Description of the Drawings does not disclose the data presented in Figure 5C.

Appropriate correction is required.

Sequence compliance

37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by

"SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application.

2. **The disclosure is objected to for the following reason:** this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences are set forth in the specification that lack sequence identifiers.

The specification is objected to because Figures 3D and 3E contain nucleic acid sequences without corresponding SEQ ID NOs in the figures nor in the figure legend. When a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier,("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings. See MPEP §2422.02.

It is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP 244.02). If the sequences are already present in the sequence listing, it would be remedial to amend the Brief Description of the Drawings or specification to include the appropriate sequence identifiers. Applicants are required to comply with all of the requirements of 37 CFR 1.821 - 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive.

37 CFR 1.821(f) states that in addition to the paper copy required by paragraph (c) of this section and the computer readable form required by paragraph (e) of this section, a statement that the content of the paper and computer readable copies are the same must be submitted with the computer readable form, *e.g.*, a statement that "the information recorded in computer readable form is identical to the written sequence listing."

Note that if the SEQ.txt file was received via EFSWeb and the text file meets the requirements for the paper copy and CRF, no statement is required.

The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

Claim Objections

3. **Claim 6 is objected to because of the following informalities**:

These claims each identify AP and TRA-1-60 as markers that are used in the claimed invention. However, the claims do not first identify the markers by their complete names prior to using their respective acronym. The abbreviation should be spelled out in the first appearance of the claims and should be followed by the abbreviation in parentheses, e.g. Epidermal Growth Factor (EGF).

The Examiner notes that if "AP" is intended to be the acronym for alkaline phosphatase, then "AP" should be placed in parentheses as was done for "SSEA-4".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. **Claims 1-5, 28 and 36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.** The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is directed to pluripotent canine embryonic stem cells. At issue for the purpose of written description requirements are those markers that identify the claimed cell as having an "embryonic stem cell phenotype", wherein said marker(s) is/are not found in

murine embryonic stem cells so that the artisan may isolate and/or enrich for the canine pluripotent embryonic stem cells from a population of mixed cell types.

> *Vas-cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification should "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L.P. vs Faulding Inc*. 56 USPQ2nd 1481 (CAFC 2000).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, the specification discloses that the embryo-derived canine embryonic stem cells express Oct-4, SSEA-4, TRA-1-60 and alkaline phosphatase (pg 8, lines 11-14), but do not express SSEA-1 (pg 20, line 38), which is found in murine ES cells (pg 26, line 23). Claim 4 is tautological in that because the cells are enriched for canine embryonic stem cells they must be immunoreactive with canine embryonic stem cells markers. However, the specification fails to disclose what genus of markers would clearly identify a given cell to be a canine embryonic stem cell, nor what markers are specifically expressed by canine embryonic stem cells but are not expressed by murine embryonic stem cells. The Examiner notes, for example, that the phenotype of indefinite proliferation *in vitro* reasonably embraces transformed

and tumorigenic cancer cells, e.g. teratomas, which are not recognized by those of ordinary skill in the art to be embryonic stem cells.

"The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (col. 3, page 71434), "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (col. 2, page 71436).

An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 1 19 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998), *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*, *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18

USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. *In Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function … does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

The Applicant has not provided any description or reduction to practice of markers that clearly identify a canine embryonic stem cell besides the expression of alkaline phosphatase, SSEA-4, TRA-1-60 and Oct-4, and the absence of SSEA-1, a marker expressed in murine embryonic stem cells. Based on the Applicant's specification, the skilled artisan cannot envision the genus of undisclosed markers that would clearly identify a given cell as being a canine embryonic stem cell, as well as those markers that are expressed in canine embryonic stem cells but not expressed in murine embryonic stem cells encompassed by the claims. How is the artisan to isolate and/or enrich a canine pluripotent embryonic stem cell from a population of mixed cell types in the absence of knowing what markers specify the desired cell type?

Thus, for the reasons outlined above, it is concluded that the claims do not meet the requirements for written description under 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. **Claims 1-4 are rejected under 35 U.S.C. 102(b)** as being anticipated by Stice et al (U.S. Patent 5,994,619).

The claims are drawn to pluripotent embryonic stem cells isolated from *in vitro* treatment of canine embryos. The instant specification discloses the term "embryo" to encompass "a developing cell mass that has not implanted into the uterine membrane of a maternal host. The term may refer to a fertilized oocyte, a pre-blastocyst stage developing cell mass, a blastocyst, and/or any other developing cell mass that is at a stage of development prior to implantation." (pg 7, lines 25-28).

Stice et al disclose cultured inner cell mass cells capable of producing transgenic animals (Abstract). The ICM cells are obtained from a blastocysts or a pre-blastocyst stage embryo (col. 6, lines 21-24) from a canine source (col. 10, line 62) and cultured *in vitro* (col. 8, lines 44-49). The cells express cell markers identically or substantially similarly to that of the ICM of developing embryos (col. 4, lines 63-65). Suitable cell markers to identify the inner cell mass cells include alkaline phosphatase (col. 8, line 67) and Oct-4 (col. 9, lines 10-11).

While Stice et al do not disclose *ipsis verbis* that the cells "are capable of indefinite proliferation in vitro in an undifferentiated state", Stice et al do disclose that the cells maintain the desired morphological and cell marker properties for prolonged periods in tissue culture, i.e. after repeated passaging, theoretically indefinitely (col. 14, lines 2-5; col. 15, lines 10-14).

Thus, Stice et al anticipate the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. **Claims 5-6 are rejected under 35 U.S.C. 102(b)** as anticipated by or, in the alternative, **under 35 U.S.C. 103(a)** as obvious over Stice et al (U.S. Patent 5,994,619).

Stice et al disclose cultured inner cell mass cells capable of producing transgenic animals (Abstract). The ICM cells are obtained from a blastocysts or a pre-blastocyst stage embryo (col. 6, lines 21-24) from a canine source (col. 10, line 62) and cultured *in vitro* (col. 8, lines 44-49). The cells express cell markers identically or substantially similarly to that of the ICM of developing embryos (col. 4, lines 63-65). Suitable cell markers to identify the inner cell mass cells include alkaline phosphatase (col. 8, line 67) and Oct-4 (col. 9, lines 10-11).

Applicant has claimed cells comprising markers TRA-1-60 and SSEA-4, as well as markers not found in murine embryonic stem cells, e.g. SSEA-1. However, it appears that the instantly claimed cells are the same as the prior art cells, given that each has the alkaline phosphatase and Oct-4 markers recognized in the art as common embryonic stem cell markers.

Alternatively, if the instantly claimed cells of the instant invention are not identical to the inner cell mass cells of Stice et al, then it appears that the canine inner cell mass cells of Stice et al only differs from the instantly claimed cells due to minor morphological variation, wherein said minor morphological variation would be expected to occur in different cells of the embryo-derived inner cell mass when cultured *in vitro* under the appropriate conditions, and wherein said minor morphological variation would not confer a patentable distinction to embryo-derived cells because Stice et al disclose that the embryo-derived inner cell mass cells are capable of developing into whole animals, which is the art-recognized **functional definition of embryonic stem cells**. Thus the claimed invention was *prima facie* obvious as a whole to one of ordinary skill in the art at the time it was made, if not anticipated by the inner cell mass cells of Stice et al.

7. **Claims 28-36 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Stice et al (U.S. Patent 5,994,619), as applied to claims 1-6 above, and in further view of Carpenter et al (U.S. 2002/0019046 A1).

Determining the scope and contents of the prior art.

Stice et al do not disclose:

i) a pharmaceutical composition comprising embryonic stem cells or cell preparations of any preceding claim according to claim 2 and a pharmaceutically acceptable carrier, excipient, or diluent, and

ii) a kit comprising embryonic stem cells as claimed in any claim 2 and instructions for their use.

However, at the time of the invention, Carpenter et al disclosed a kit with instructions for use, wherein the kit comprised embryonic stem cells and a pharmaceutically acceptable carrier ([0045], [0155]).

Ascertaining the differences between the prior art and the claims at issue, and Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in embryology, *in vitro* fertilization, cell biology and the creation of transgenic cells and organisms. Therefore, the level of ordinary skill in this art is high.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine a composition comprising pluripotent embryonic stem cells obtained from canine embryos (Stice) with a pharmaceutically acceptable carrier, and a kit comprising said composition, said kit further comprising instructions for use (Carpenter) with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to combine a composition comprising pluripotent embryonic stem cells obtained from canine embryos with a pharmaceutically acceptable carrier, and a kit comprising said composition, said kit further comprising instructions for use because said canine embryonic stem cells may be used for cell transplantation and/or cell therapy, and it is common practice in the art to provide cells in kit form along with an acceptable carrier and instructions for use.

Thus, absent evidence to the contrary, the invention as a whole is *prima facie* obvious.

Conclusion

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill, Ph.D./
Examiner, Art Unit 1633

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633